

## REMARKS

### Status of Claims

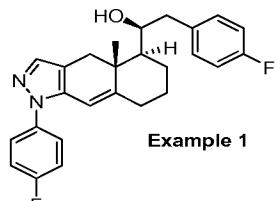
Claims 8-14 and 22 are pending in the application prior to the instant Response. No claim is amended, added or canceled, leaving claims 8-14 and 22 pending upon entry of the instant Response.

Indication of Allowability - Applicants acknowledge the examiner's indication of allowability of claims 11-14.

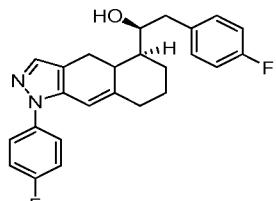
### Rejections under 35 U.S.C. §103(a)

At page 2 of the Office Action, the Examiner rejected claims 8-10 and 22 under 35 U.S.C. §103(a) as being obvious over Ali et al. (WO 04/075840), Ali et al. (WO 04/026248) and Ali et al. (WO 2003/086294; hereinafter, "Ali").

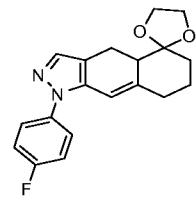
The Examiner also appeared to allege that a skilled artisan would have been motivated to modify Example 1 of Ali (hereinafter, "Ali Compound") to obtain its homolog compound (hereinafter, "Homolog Compound") which can be used for the synthesis of the instant compound of the following structure (hereinafter, "Instant Compound"):



Ali Compound



Homolog Compound

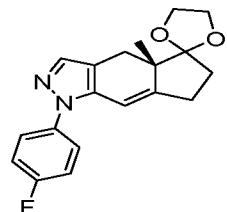


Instant Compound.

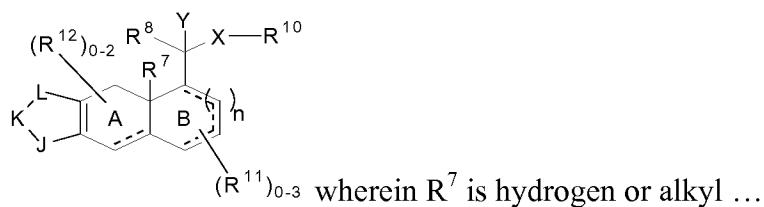
In particular, the Examiner alleged that (bold face and text in square brackets added for better illustration):

#### Determination of the Scope and Contents of prior art.

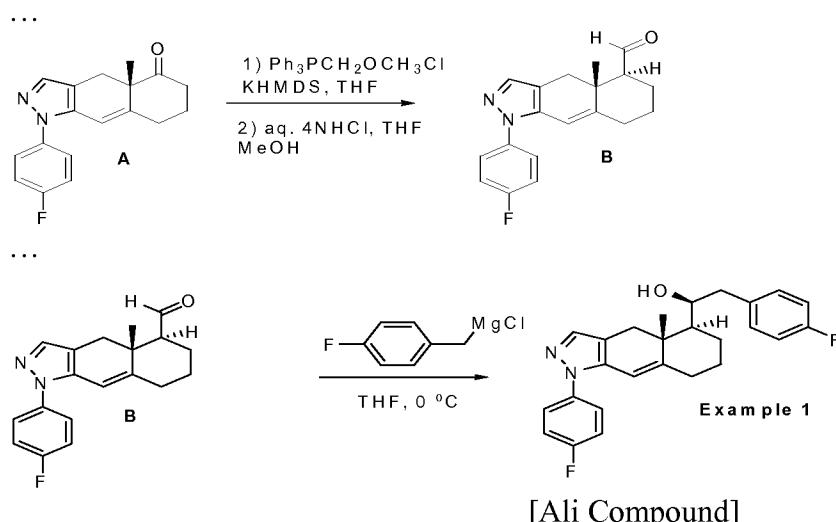
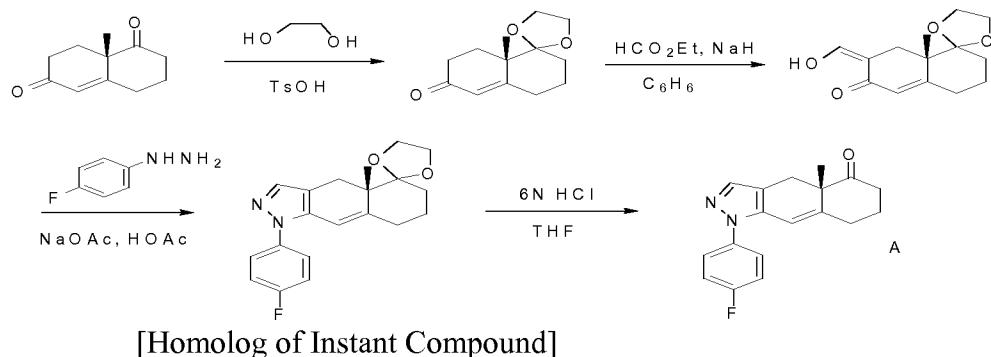
The references teach the compound shown below ...



The compound is an intermediate in the synthesis of final product

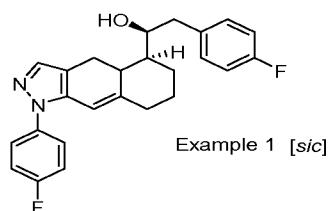


For example,



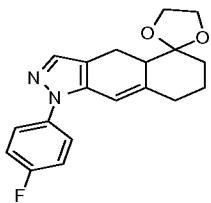
Ascertaining the differences between prior art and instant claims.

**The following generically taught modification to prior art final product (i.e. homolog)**



[Homolog Compound]

**results in the synthesis of a composition comprising**



[Instant Compound]

**which is within the scope of the instant claims.**

(Office Action mailed January 7, 2009, pages 3-4)

The Examiner also alleged that a skilled artisan would be motivated from the prior art disclosure to make the modifications required to arrive at the instant invention with reasonable expectation of success:

One of ordinary skill would be motivated, from the prior art disclosure – ie. generic teaching and the preferred embodiment - to make the modification required to arrive at the instant invention with reasonable expectation of success for obtaining an additional compound for the same utility. The motivation would be to make an additional glucocorticoid receptor modulators [*sic*].

(Office Action mailed January 7, 2009, page 5) Applicants respectfully traverse this rejection as the examiner has not made out a *prima facie* case of obviousness in view of the cited references.

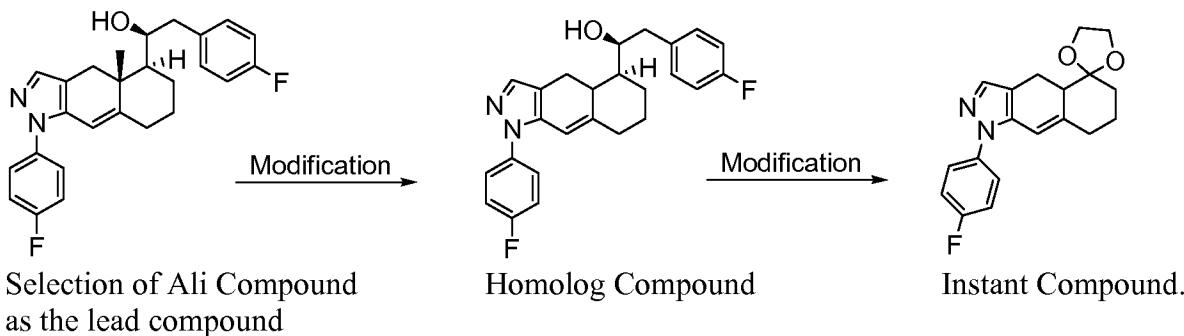
Courts have consistently held that a *prima facie* case of obviousness as related to a new chemical compound requires that the prior art provide some suggestion or motivation for making the specific molecular modifications necessary to achieve the claimed invention combined with a reasonable expectation of success. *Takeda v. Alphapharm*, 492 F.3d 1350, 1356 (Fed. Cir. 2007). The court made it clear that "consistent with the legal principles enunciated in *KSR*", there must be "some reason that would have led a chemist to modify a known compound in a particular manner." *Id* at 1356-1357.

Additionally, courts also made it clear that "post-*KSR*, a *prima facie* case of obviousness for a chemical compound still, in general, begins with the reasoned identification of a lead compound. *Teva* cannot create a genuine issue of material fact on obviousness through the unsupported assertion that compounds other than landsoprazole might have served as lead compounds". *Eisai v. Dr. Reddy's*, 533 F.3d 1353, 1359 (Fed. Cir. 2008).

Here, the chemical art of the instant application is both unpredictable and vast. The Examiner's assertion that "[o]ne of ordinary skill would be motivated, from the prior art

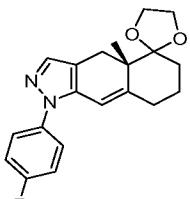
disclosure – ie. generic teaching and the preferred embodiment - to make the modification required to arrive at the instant invention" is simply unsupported by the teachings of the cited references. These references, either alone or in combination, fail to identify the Ali Compound as the lead compound for further modifications. Moreover, the references also fail to provide any suggestion or motivation to make the particular molecular modifications necessary to arrive at the Instant Compound from the Ali Compound.

To arrive at the Instant Compound from the Ali Compound as alleged by the Examiner, a skilled artisan would need to reverse the reaction steps of Ali and do the following modifications. First, a skilled artisan would have to select the Ali Compound as the lead compound for further modifications. Second, the skilled artisan would have to modify the Ali Compound in the particular way required to obtain the Homolog Compound. And third, the skilled artisan would further have to modify the Homolog Compound in the particular way required to arrive at the Instant Compound. The required steps are illustrated below:



As a general matter, the Examiner's position that a skilled artisan would have been motivated to select the Ali Compound as the lead compound, reverse the reaction steps of Ali and modify the Ali Compound through the Homolog Compound in the particular way required to arrive at the Instant Compound is contrary to the teachings of the cited references.

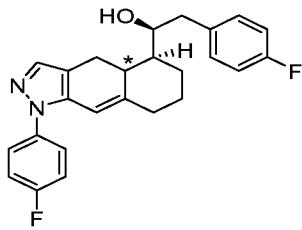
The Ali Compound (i.e., ) is disclosed in Ali as a reaction product and an active compound possessing selective glucocorticoid receptor activity (Ali, pages 42-28, Example 1; page 159, lines 13-14). On the other hand, a homolog of the Instant Compound



(i.e., F ) is disclosed in Ali solely as a synthetic intermediate for making the Ali Compound (Ali, page 42, line 1-9). There is no disclosure whatsoever in the cited references that the synthetic intermediate or any of its homolog compounds possesses any selective glucocorticoid receptor activity. Additionally, a skilled artisan would have no reason to believe that the synthetic intermediate would have any activity since this compound has vastly different chemical structure than those of the active compounds disclosed in Ali. Thus, there would be no reason or motivation for a skilled artisan to select the Ali Compound, an active compound, as a lead compound, reverse the synthetic steps, and modify it to obtain a synthetic intermediate (or its homolog) whose activity is totally unknown.

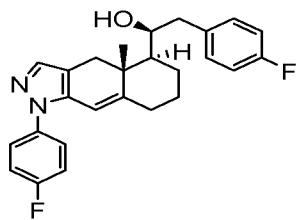
Even assuming, *arguendo*, that Ali would have motivated a skilled artisan to reverse the reaction steps of Ali, which it did not, the artisan would not have selected the Ali Compound as the lead compound. Ali (WO 2003/086294) discloses the Ali Compound (page 48, Example 1) among more than two hundred active compounds any one of which could have been selected as a lead compound for further investigation. There is no teaching or suggestion in Ali that the Ali Compound possesses any superior property over the rest of the compounds and thus there would have been no reason or motivation to select this compound as the lead compound.

Moreover, there is no teaching or suggestion in the cited references that the Ali Compound be modified through the Homolog Compound to arrive at the Instant Compound. The Homolog Compound is un-substituted at the position marked with an asterisk on the three-ring core structure (asterisk "\*" added for better illustration):



(Homolog Compound).

On the other hand, the Ali Compound is methyl substituted at the same position:



(Ali Compound).

It appears to Applicants that all disclosed and claimed active compounds in Ali that share the same three-ring core structure are methyl substituted at the same position. Thus, a skilled artisan would readily appreciate that the presence of the methyl group at this particular position is an important feature for the intended selective glucocorticoid receptor activity. Thus, the skilled artisan would not have been motivated to modify the Ali Compound to obtain the Homolog Compound as doing so would have resulted in a compound not having an important feature (methyl substitution) as taught by Ali.

Furthermore, there would have been no reasonable expectation of success for the alleged modifications from the Ali Compound to the Instant Compound. Ali only discloses synthetic routes and conditions from the synthetic intermediate (a homolog of the Instant Compound) to the Ali Compound. It does not in any way teach or suggest that the synthetic routes are reversible and does not disclose any routes or conditions for a reverse process. There also is no indication that the process of modifying the Ali Compound to the Instant Compound through the Homolog Compound was a routine process at the time of the instant invention. Therefore, a skilled artisan would not have known what synthetic routes and conditions to use to arrive at the Instant Compound from the Ali Compound.

Applicants respectfully point out that the Examiner appeared to have used hindsight analysis using the instant application as the source of teachings or suggestions to arrive at the applicants' own invention. This kind of hindsight analysis is not permitted by the patent law.

**Claim 22** - Claim 22 depends from allowable Claim 11 and further requires that the pharmaceutical composition comprise a pharmaceutically acceptable carrier. Since claim 11 is novel and has been allowed, its dependent claim 22 also is novel over the cited references. Accordingly, Applicants respectfully request withdraw of the §103(a) rejection and allowance of this claim.

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In view of the foregoing remarks, Applicants respectfully request reconsideration of the pending claims and reexamination of the application. Timely allowance of the pending claims is respectfully requested.

The Examiner is invited to contact the undersigned attorney at the telephone number provided below if such would advance the prosecution of the instant application. Applicants believe no additional fees are due, but the Commissioner is authorized to charge any fees required in connection with this Response from Merck Deposit Account No. 13-2755.

Respectfully submitted,

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Date: April 2, 2009